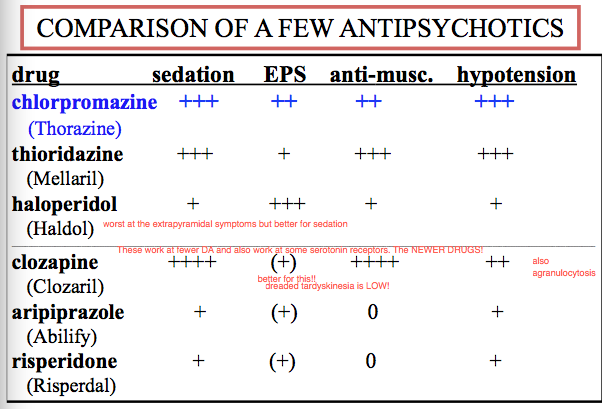
* **RESPIRATORY**
  + **Β-AGONISTS**
    - **EPINEPHRINE**
    - **TERBUTALINE**
    - **ALBUTEROL**
    - **SALMETEROL**
  + **ANTICHOLINERGICS**
    - **IPRATROPIUM BROMIDE**
  + **GLUCOCORTICOIDS**
    - **PREDNISONE**
    - **PREDNISOLONE**
    - **METHYLPREDNISOLONE**
    - **TRIAMCINOLONE**
    - **TRIAMCINOLONE ACETONIDE**
    - **BECLOMETHASONE**
    - **FLUTICASONE**
  + **LEUKOTRIENE RECEPTOR ANTAGONISTS**
    - **ZAFIRLUKAST**
    - **MONTELUKAST**
  + **5-LO INHIBITORS**
    - **ZILEUTON**
  + **METHYLXANTHINES**
    - **THEOPHYLLINE**
  + **MAST CELL STABILIZERS**
    - **CROMOLYN SODIUM**
  + **PROSTAGLANDINS**
    - **EPOPROSTENOL**
  + **ENDOTHELIN ANTAGONISTS**
    - **BOSENTAN**
  + **OPIOID AGONISTS**
    - **CODEINE**
    - **DEXTROMETHORPHAN**
  + **EXPECTORANTS**
    - **GUAIFENESIN**
* **NON-SELECTIVE CNS DEPRESSANTS**
  + **BARBITURATES**
    - **THIOPENTAL**
    - **PENTOBARBITAL**
    - **SECOBARBITAL**
    - **BARBITAL**
    - **PHENOBARBITAL**
  + **OTHERS**
    - **PROPOFOL**
    - **ETOMIDATE**
    - **KETAMINE**
    - **NON-BARBITURATE SEDATIVE HYPNOTICS—CHLORAL HYDRATE**
* **LOCAL ANESTHETICS**
  + **ESTERS**
    - **COCAINE**
    - **PROCAINE**
    - **BENZOCAINE**
    - **TETRACAINE**
  + **AMIDES**
    - **LIDOCAINE**
    - **BUPIVACAINE**
    - **LEVOBUPIVACAINE**
    - **ROPIVACAINE**
* **GENERAL ANESTHETICS**
  + **INHALATIONAL**
    - **HALOTHANE**
    - **ISOFLURANE**
    - **SEVOFLURANE**
    - **DESFLURANE**
    - **N2O**
  + **INTRAVENOUS**
    - **BARBITURATES**
    - **PROPOFOL**
    - **ETOMIDATE**
    - **NOT NON-SELECTIVE CNS DEPRESSANTS**
      * **OPIOIDS**
      * **BENZODIAZEPINE**
      * **KETAMINE**
* **ALCOHOLS**
  + **ETHANOL** 
    - Nonselective CNS depressant
    - Affects on GABAA (plus includes a type of this receptor in the cerebellum—ataxia), Inhibits Glu transmission, Action at NMDA receptor
    - Adverse: myocardial depression, vasodilation in CNS, peripheral vasodilation may be due to ↑ acetaldehyde
    - Fatty food delay abs
    - F>M
    - Metabolized by Alcohol DH
      * Mechanism is limited by NAD+
    - Zero order kinetics
  + **DISULFIRAM**
    - Inhibits Acetaldehyde DH🡪 accumulation of Acetaldehyde (flushing, HA, N/V, hypotension, etc)
    - Polymorphisms in this enzyme—Asians have ↓ so ↑ effects of alcohol--↑ acetaldehyde so when they drink a lot its like they are on disulfiram so they normally don't abuse alcohol
  + **METHANOL**—wood alcohol
    - Metabolized by alcohol DH🡪 formaldehyde and formic acid🡪 toxic to retina (blindness)
    - Tx: ethanol or fomeprizol
  + **ETHYLENE GLYCOL—**antifreeze
    - Metabolized by alcohol DH into axalic acid
    - Tx: ethanol or fomeprizol
  + **FOMEPIZOL—FO-ME-Pizol (FOr M-methanol and E-ethylene glycol intox)** 
    - Inhibits alcohol DH (polymorphisms in this too--↑ activity🡪 ↓ abuse)
  + **NALTREXONE**
    - Long acting Opioid antagonist—DON'T GIVE IF PT IS TAKING OPIOIDS
  + **ACAMPROSATE**

* **BENZODIAZEPINES**
  + *Functional tolerance (not metabolic) to some of the effects but NOT ALL*
  + **TRUE BENZODIAZEPINES**
    - **DIAZEPAM (VALIUM)**
      * Uses: Anxiolytic, Hypnotic, Anticonvulsant, Muscle Relax, Pre-anesthetic
      * MOA: Works at CERTAIN GABA­A receptors, binding to the benzo receptor ( γ2 subunit) ↑ their activity🡪 ↑ Cl coming in and ↑ inhibitory potential at post-syn site. GABA must be present.
      * Well abs (not IM), distributes well
        + IV—very rapid onset and short DOA due to distribution
      * COMPLICATED Biotransformation (dealk, hydroxyl🡪 3 active metabolite)
        + No induction of enzymes
        + Desmethyldiazepam is longest acting metabolite and it accumulates
        + Want to give this during WITHDRAW b/c want to give brain time to get used to drug free state
    - **FLUMAZENIL**
      * Competitive ANTAG at the BZ binding site on GABA­A receptor
      * NO action of its own
      * Uses: reversal of conscious sedation, tx of BZ OD.
    - **ANXIOLYTICS** (*all BZ’s are anxiolytic)*
      * **DIAZEPAM—**complicated biotransformation
      * **LORAZEPAM**
        + SIMPLE biotransformation!—CONJUGATION🡪 INACTIVE metabolite
      * **ALPRAZOLAM** (“antidepressant”)
        + SIMPLE biotransformation!—HYDROXYLATION then CONJUG. 🡪 Active🡪 rapidly inactive metabolite
    - **HYPNOTICS *(****↓ onset ↓ awakenings*)
      * *No tolerance develops*
      * **TRIAZOLAM—**short acting
        + SIMPLE biotransformation!—HYDROXYLATION then CONJUG. 🡪 Active🡪 rapidly inactive metabolite
      * **ZOLPIDEM—**selective for GABA­A receptor w/ an α1 subunit🡨MORE selective
      * ***\*\*better than barbiturates for sleeping!***
    - **ANTICONVULSANT (***can dev. tolerance*)
      * **DIAZEPAM—**medical emergency
        + Works fast
      * **LORAZEPAM**—medical emergency
        + longer action than diazepam
      * **CLONAZEPAM—**chronic tx
        + COMPLICATED BIOTRANSFORM.
    - **MUSCLE RELAXANT**
      * **DIAZEPAM—**↓ skeletal mm. tone
    - **PREANESTHETIC** *tolerance develops* 
      * **DIAZEPAM—**rapid recovery after single IV dose due to DISTRIBUTION
      * **MIDAZOLAM**—induction, not true anesthetic state
        + SIMPLE biotransformation!—HYDROXYLATION then CONJUG. 🡪 Active🡪 rapidly inactive metabolite
        + rapid recovery after single IV dose due to BIOTRANSFORMATION
  + **NON-BENZODIAZEPINE HYPNOTICS**
    - **ZOLPIDEM (AMBIEN)**
    - **RAMELTON (**RAMEY HAS A CRAZY SLEEP SCHEDULE (DSPS) SO HE TAKES MELATONIN, HE ACTS LIKE HES 12 girl (↓ TESTESTERONE ↑ prolactin)
      * Melatonin Agonist—promotes sleep
      * Indicated for Delayed sleep phase syndrome (DSPS)—circadian rhythm disorder
      * Metabolised by CYP1A2
      * Drug interactions: inhibited by fluvoxamine, INDUCED by rifampin
      * Adverse: ↓ testosterone, ↑ prolactin
  + **NON-BENZODIAZEPINE ANXIOLYTICS**
    - **BUSPIRONE—**I HAVE ANXIETY ABOUT TAKING THE BUS AND NOT MY BENZ!!
      * Partial agonist at 5-HT1A receptors
      * 1-3 weeks until onset of effects
      * drug interactions—HTN w/ MAOI—KIDS IN GRADES 3 & 4 CANT TAKE THE BUS SO MA (MAO) HAS TO TAKE THEM
        + interactions also w/ drugs that induce or inhibits CYP3A4 (it is metabolized by this)
* **PARKINSON’S DRUGS**
  + *↓ DA neurons in the substantia nigra pars compacta (↓ in nigrostriatal pathway) 🡪 ↓ inhibitory signaling from striatum to the SNpr/GPi🡪 ↑ activity of the SNpr/GPi (which is inhibitory) so ↑ inhibition to the thalamus🡪↓ cortical sitimulation 🡪 ↓ movements*
  + *Toxin induced Parkinsonism—MPTP!!*
  + **SUPPLY SUBSTRATE** 
    - **DOPAMINE**
      * Does not cross BBB
    - **LEVADOPA**
      * Transported into neurons and decarbox into DA by L-AAAD (DOPA DECARBOXYLASE)🡪 concentration in synaptic vesicles
        + This enzyme is widely distributed in intestinal mucosa so NEED TO GIVE A DECARBOXYLASE INHIBITOR (want the levodopa to get to brain—1-3% of the dose gets into the CNS)

Adverse effects—CV system (tachy, arrhythmias), nausea

* + - * For this drug to be effective some nigrostriatal neurons must still be alive—effects will ↓ as disease progresses
      * Abs—effected by rate of gastric emptying and gastric pH
      * Worsening of sx’s near the end of the dose interval.
      * ON-OFF phenom—bradykinesia🡪 dyskinesia
      * Adverse: N/V, anorexia, SNS, Dyskinesias, Behavioral
      * Drug interaction—**MAOI🡪 HTN,** antipsychotic drugs (that block DA receptors--↓ levodopa effect), anticholinergic drugs
      * Inhibitors of COMT ↓ levodopa metabolism 🡪 on period lengthen (↑ drug effects)
    - **CARBIDOPA**
      * Inhibits the aromatic-L-amino acid decarbox—does NOT cross BBB
      * This is the one given w/ levodopa to prevent metabolism before it gets into the brain
  + **INHIBIT DA BREAKDOWN**
    - **SELEGILINE**
      * MAO-B INHIBITOR (blocks DA breakdown)
        + Nonselective MAOI + levodopa🡪life threatening
      * ↑ the CNS effects of levodopa (good and bad effects)
  + **POSYSYNAPTIC DA AGONIST**
    - **BROMOCRIPTINE**
      * DA-agonist
      * Also useful in Tx AMENORRHEA-GALACTORRHEA associated w/ hyperprolactinemia (prolactin secreting tumor)
        + Pituitary cells that release prolactin receive DA inhibition
    - **PRAMIPEXOLE & ROPINIROLE**
      * some selectivity for D2-like receptors (DA2 and DA3)
      * Alone or in combo w/ levodopa/carbidopa
      * Ropinirole is also approved for restless leg syndrome
      * Longer DOA than levodopa
      * Adverse: orthostatic hypotension, N/V, anorexia, dyskinesias, mental disturbances
  + **PROMOTE DA RELEASE**
    - **AMANTADINE**
      * Stimulate presyn release of DA
      * Used alone in early stages
      * Benefits are short lived
  + **DRUGS THAT INHIBIT CHOLINERGIC NEUROTRANSMISSION IN THE STRIATUM**
    - **BENZTROPINE**
      * Atropine-like but w/ better ration of CNS:PNS effects
      * Used for ANTIPSYCHOTIC DRUG –INDUCED PARKINSONISM
* **CNS STIMULANTS**
  + **METHYLXANTHINES**
    - Heart actions—positive inotropic and chronotropic effects (arrhythmias at ↑ doses)
    - Vessel-↓ R systemically, ↑ cerebral R
    - Diuresis, stimulate gastric acid secretion, metabolic effects (↑ BMR), skeletal muscle (↑ contractile strength at very high conc; ↓ doses for this if you have COPD)
    - Poor water solubility—abs slow
    - Demethylated in liver and oxidized
    - Readily penetrate BBB and placenta
    - **CAFFEINE**
      * Competitive ANTAGonists at ADENOSINE receptors—adenosine is inhibitory NT
      * ↑ doses—inhibit PDE
      * Effects: ↓ fatigue, ↓ reaction time, ↑ awareness of sensory stimuli, ↑ performance on some tasks, can stimulate respiration at ↑ doses
      * Adverse: nervousness, insomnia
      * Use: tx cerebrovascular HA (b/c in this the vascular is dilated and you want to ↑ R)
      * Widely abused
      * Dependence—HA, lethargy, irritability
    - **THEOPHYLLINE**
      * Used to tx asthma but narrow therapeutic index
      * Actions: diuresis
      * Adverse--convulsions are possible
      * Poor water solubility so inject (theophylline salts)
      * No tolerance to bronchial SM effects
  + **SYMPATHETOMIMMETICS**
    - **AMPHETAMINES—**release NE and DA
      * Substrate of DAT so competitively inhibits DA transport. In the cell it alters the VMAT and impedes the filling of synaptic vescicles🡪 cytoplasmic DA ↑ 🡪 reversal of DAT so expel DA🡪 ↑ extracellular DA
      * Actions: ↑ alertness, wakefulness, ↓ fatigue, ↓ distractibility, anorexia, euphoria, ↑ inner sense of well-being
      * Adverse: HTN, Tachy, premature beats, hyperactive DTR, tremor, weight lood
      * Tolerance—CNS actions some CV actions
      * High abuse liability associated w/ addiction and binge use (similar to cocaine) but little or no dependence
      * Medical Uses: ADHD, Narcolepsy, Weight Loss
      * **DEXTROAMPHETAMINE**
        + D-isomer 🡪 greater potency for CNS than PNS effects
      * **METHYLPHNEIDATE (RITALIN)**
        + Similar to Dextroamphetamine
    - **COCAINE**
      * Inibits DAT🡪 ↑ extracellular DA
        + Also inhibit reuptake of NE & 5-HT
      * Tox: CV—tachy, arrhythmias, angina, infarct, ICH, Seizures, obstetric complications (premature separation of the placenta), ENT findings (nasal ulceration)
      * High abuse liability associated w/ addiction, dependence is minimal
        + Craving for drug—dysphoria, psychic depression, sleepiness, fatigue, bradycardia
      * Base form—CRACK
      * Acid—SNORT FORM
* **ANTI-PSYCHOTICS**
  + THOR washed his CLOZs in CHLORox wearing nothing but a HALO...b/c, you know, he thought he was Thor but was really just a crazy naked schizo at the laundromat. (Thioridazine, Clozapine, Chlorpromazine, Haloperidol)
  + **Psychoses**: Schizophrenia, depression, bipolar disorder, schizo-affective, Korsakoff's syndrome, toxic psychosis (from amphetamines, phencyclidine, or steroids)
    - Korsakoff caused by a lack of thiamine (vitamin B1) in the brain. Linked to chronic alcohol abuse and/or severe malnutrition. There are 6 major sx: anterograde amnesia, retrograde amnesia, severe memory loss confabulation, (invented memories which are then taken as true due to gaps in memory sometimes associated with blackouts), meager content in conversation, lack of insight, apathy (the patients lose interest in things quickly and generally appear indifferent to change)
  + Actions
    - Work at 5-HT receptors, Muscarinic R, α adrenergic R, Histamine R, and of course DA receptor
    - Suppression of psychotic sx
      * b/c competitive antag of DA receptors on neurons receiving mesolimbic or mesocortical innervation
      * esp in pts w/ schizo (+ symptoms respond best; - symptoms respond less)
    - Acute neurotoxicities (extrapyramidal signs;EPS)—antagonistic effects of DA receptors in striatal neurons🡪 ↓ nigrostriatal transmission (parkinsonism)
      * Not seen in atypical/newer drugs
    - Tardive dyskinesia (oral and facial dyskinesias, choreoathetosis and/or dystonia)—late appearing dyskinesias. Takes months or years for this to appear!—seem like ↑ sensitivity to DA (↑ regulation of DA receptors after prolonged therapy)
      * DON'T LET THIS HAPPEN!
      * Rare w/ atypical drugs
    - Neuroleptic malignany sx—rare but fatal
      * Parkinsonism + catatonia, autonomic instability, hyperthermia and stupor
      * Tx: cooling, diazepam or dantolene
    - Atropine-like action: blockade of muscarinic receptors (dry mouth, dry skin, tachy, difficult urination)
    - Orthostatic hypotension—especially drugs that are strong blockers of α adrenergic receptors (chlorpromazine)—tolerance
    - Sedation—possibly b/c of block of H1 receptors
    - Endocrine effects—block of DA receptors in hypothalamus and pituitary—PROLACTIN SECRETION IS STIMULATED
    - Results—false positive pregnancy test, gynecomastia, galactorrhea, ↑/↓ libido
    - Sexual dysfunction in both men and women
    - Antiemetic effect—block of DA receptors in chemoreceptor trigger zone
    - Seizures--↓ threshold
    - Hypersensitivity rxn
    - Eye problems
    - Cardiac toxicities
    - 
  + **TYPICAL (FIRST-GENERATION): D2 RECEPTOR ANTAGONISTS**
    - **PHENOTHIAZINES**
      * **ALIPHATIC: CHLOROPROMAZINE**
        + Effect:
        + α-adrenergic receptor agonist activity🡪 hypotension
        + Antiemetic effect—block of DA receptors in chemoreceptor trigger zone
        + ↑ hypersensitivity rxns
      * **PIPERIDINE: THIORIDAZINE**
        + Not anti-emetic
        + ↑ doses can cause retinal deposits
        + ↑ doses associated w/ T wave and QT abnormalities and can produce fatal ventricular arrhythmias
      * **PIPERAZINE: FLUPHENAZINE**
        + Antiemetic effect—block of DA receptors in chemoreceptor trigger zone
    - **BUTYROPHENONES**
      * **HALOPERIDOL**
  + **ATYPICAL (SECOND-GENERATION): 5HT2 >D2 BLOCK**
    - These have fewer DA (DA4) receptors involved and only one kind of serotonin receptor (2A) is antagonized
    - 5-HT receptor role🡪 lead to weight gain
    - used to tx levodopa psychosis
    - ↑ blood sugar, ↑ lipids and cholesterol, ↑ weight gain
    - ↓ EPS and ↓ tardative dyskinesias
    - **INDOLES**
      * **CLOZAPINE**
        + ↑ frequency of Agranulocytes
      * **RISPERIDOL**
      * **ARIPIPRAZOLE**
  + **Drug interactions w/ Antipsychotics**
    - Additive CNS depression
    - Additive anticholinergic effect
    - Additive quinidine like effects on the heart (thioridazine)
    - Block effectiveness of levodopa in parkinson’s dz (less in newer drugs)
    - Block amphetamine psychosis
    - Seizure threshold is ↓ --danger for epileptics or in sedative-hypnotic or ethanol withdrawal
* **OPIOIDS**
  + **MORPHINE**
    - Opioid Receptors are g-protein coupled (mostly Gi/Go) and are located mostly in CNS and GIT
      * Presynaptic opioid receptors ↓ Ca conductance while postsynaptic opioid receptors ↑ K+ conductance
      * Subtypes:
        + **MU—(MORPHINE SITE OF ACTION AND MOST OTHER OPIOID ANALGESICS)**
        + **KAPPA—**PENTAZOCINE (THE KAPPAS HAVE A PENT HOUSE HAVE YOU ‘CINE’ IT??
        + **DELTA**
      * Opioid AGONISTS—inhibit the local circuit inhibitory neuron🡪 DISINHIBITS the INHIBITORY PAIN NEURON (so now the inhibitory pain neuron is active)
    - ACTIONS
      * Analgesia (↑ pain threshold, changes subjective response to pain)
      * Euphoria/Dysophoria—determined by expectation, route of admin, previous experience, presence of pain
      * ↓ anxiety
      * ↓ consciousness—dose dependent
        + ↓ doses—sedation (mental clouding)
        + ↑ doses—LOC, coma
      * Respiratory depression—↓ sensitivity to CO2 (↑ PaCO2, ↑ CBF). This is what kills you in OD
      * Cough Suppression (depresses cough reflex)
      * Constriction of pupils (miosis)
        + Hypoxemia causes dilation so if morphonine OD patient becomes hypoxic the pupils will be dilated
        + ↑ PSNS output to pupil
      * Truncal Rigidity—only seen in very high doses
      * N/V—activated chemoreceptor trigger zone, also a vestibular component
      * Cardiovascular—mild bradycardia, hypotension in OD or compromised C-V system patient, ↑ intracranial BF and ↑ CSF pressure, relieves dyspnea in pulmonary edema, ↑ histamine release (curare can also cause this)
      * GIT--↑ resting tone, ↓ peristalsis, ↓ secretions, ↓ sphincter tone-🡪 CONSTIPATION (may be limiting factor in tx patients)
      * ↑ biliary tone
      * GU tract--↓ renal function, ↑ ADH—transient ↓ in urine product, ↑ tone of ureter bladder and sphincter, prolonged labor
      * ↓ GnRH and CRH-🡪 ↓ in LH, FSH, ACTH and β-endorphin
      * ↑ prolactin and ADH
      * ↓ body temp
    - PHARMACOKINETICS
      * Liver is good at glucuronidating morphine to M-3-G
      * Large first-pass effect🡪 limited bioavailability
    - **SIMILAR DRUGS (**just differ in potency)**: OXYMORPHONE (more potent)**
    - May need to treat withdrawal w/ clonidine (↓ ANS)
      * 8-14 hrs—restless
      * 16-18 hrs—lacrimation, rhinorrhea, perspiration, yawning
      * 24 hrs—chills, gooseflesh, mescle cramps, mydriasis, mild HTN, hyperpnea, hyperthermia, twitches, involuntary kicking
      * 36 hrs—N/V/D gagging
      * 72 hrs—symptoms begin to stop
  + **ETROPHINE**
    - Imobilon—animal tranquilizer
    - 10000x’s more potent than morphine b/c 10000x’s more affinity for my receptors
  + **HEROIN (DIACETYLMORPHINE)**
    - Low affinity for mu receptor. It gets metabolized to monoacetylmorphine which has ↑ mu affinity—crosses BBB🡪 metabolized to morphine
    - 3-5x’s more potent than morphine
  + **CODEINE (3-METHOXY-MORPHINE)** 
    - 1/12th potency of morphine but EQUAL cough suppressant
    - Dysphoria w/ ↑ doses
    - 10% is converted to morphine🡪 analgesia
    - Polymorphism in CYP2D6
      * 10% resistant to codeine (not metabolized to morphine)
      * 5% get excessive response
  + **HYDROCODONE**
    - Metabolized to hydromorphone (morphine like) by CYP2D6
    - Hydromorphone may accumulate in patients w/ renal failure
    - Combo w/ acetaminophen (Vicoden)
  + **DEXTROMETHORPHAN**
    - Effective antitussive
    - NO analgesic
    - High doses can cause CNS effects
  + **MEPERIDINE (DEMEROL)**
    - Fast onset
    - Short DOA
    - Used in pregnancy or cleaning wounds!
    - Atropine like action (pupillary constriction)
    - Less constipation
    - No significant anti-tussive activity
    - Toxicity—respiratory distress, ↓ consciousness
    - Toxic due to metabolite—normeperidine🡪 CNS excitation, convulsions, delirium
    - INTERACTION W/ MAOI (fever, HTN, coma, severe respiratory depression)
  + **FENTANYL**
    - MU receptor agonist (80-100x’s morphine potency)
    - Short DOA b/c of distribution/redistribution
    - Used: IV analgesia and to reduce consciousness
      * Transdermal patch (FOR CANCER PATIENTS TO TX BREAKTHROUGH PAIN)**,** transmucosal formulation, transbuccal form
  + **METHADONE**
    - Slower biotransformation than morphine so it accumulates (so w/ repeated doses ↑ duration of analgesia) –long acting
    - Special uses: TREAT OPIOID ABUSE
      * Acute: substitute for usual drug then slowly reduce (avoid withdrawal sx)
      * Chronic: “maintence” programs. Sub it for usual drug then slowly RAISE dose to produce ↑ tolerance🡪 goal is to preclude any effect should the subject take an opioid agonist
  + **OXYCODONE**
    - more potent than codeine
    - metabolized to oxymorphone by CYP2D6—metabolite may accumulate in patients w/ renal failure
    - Time-release tablets (if you chew them you defeat the purpose)
  + **TRAMADOL**
    - Weak opioid agonist
    - Low analgesic efficacy
    - Action due to opioid receptor action & inhibition of SERT! (maybe also a little NET)
    - Size effect: SEIZURES
  + **D-PROPOXYPHENE (JUST KNOW NAME)**
    - Not used anymore
  + **ENDOGENOUS OPIOPEPTINS**
    - **MET-ENKEPHALIN**
      * Proenkephaline derived
      * Like a NT
    - **β-ENDORPHIN**
      * Pro-opiomelanocortin derived (POMC)
      * Acts like a hormone. Mostly in the pituitary and hypothalamus and released into bloodstream
  + **LOW PC, DON’T CROSS BBB**
    - **DIPHENOXYLATE**
      * Poor solubility, poor BBB penetration
      * Used to control diarrhea
      * Low abuse liability
    - **LOPERAMIDE (IMODIUM)**
      * Even Lower abuse liability
  + **OPIOID ANTAGONISTS**
    - **NALOXONE**
      * Competitive antagonist at ALL opioid receptors
      * W/ pts who are dependent will ppt an immediate withdrawal sx
      * No matter how much naloxone you use will just shift PCO2 toward normal when using it will morphine
      * Short DOA
      * First pass biotransformation—not effective orally
    - **NALTREXONE**
      * Oral and longer acting
    - **NALMEFENE** 
      * Longer-acting
  + **PARTIAL-MIXED AGONISTS/ANTAGONISTS**
    - **PENTAZOCINE**
      * Mixed agonist-antag
        + Kappa-agonist
        + Mu-antag
      * May ppt withdrawal (ANS hyperactivity)
        + May need to treat withdrawal w/ clonidine (↓ ANS)
      * ↑ dose you get kappa receptor response (dysphoric, psychotomimetric actions)
      * ↑ BP (so don't use in patients w/ heart problems)
    - **NALBUPHINE**
      * + Kappa-agonist
        + Mu-antag
    - **BUTORPHANOL**
      * + Kappa-agonist
        + Mu partial agonist
    - **BUPRENORPHINE**
      * + Kappa-antagonist
        + Mu partial agonist
      * Used in MAINTENANCE tx of heroine (must have the pt detox first)
        + It's a long acting drug

**ANTIDEPRESSANTS/ANTI-MANICS**

*Depression is thought to be related to ↓ NE and/or 5-HT neurotransmission*

*-Slow responses—changes in gene expression (use CREB, ↑ expression of BDNF)*

*-all drugs have delayed onset of therapeutic effects*

*-↑ incidence of suicide*

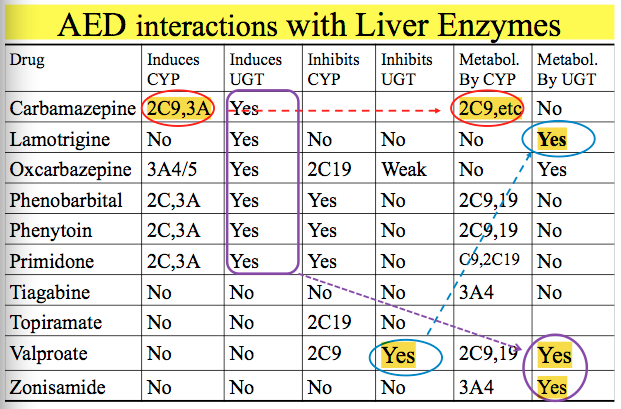
* **INHIBIT NE REUPTAKE 🡪 ↑ NE IN SYNAPTIC CLEFT**
  + *Other uses for amine reuptake inhibitors is –PTSD, OCD, Social anxiety disorder, generalized anxiety disorder, panic disorder, pain disorders, prementral dysphoric disorder (SSRI), smoking cessation, Bulimia (not anorexia), bed wetting*
  + **TRICYCLIC (1ST GENERATION)**
    - *The TCA’s lead to β and α2 receptor down regulation*
    - **AMITRIPTYLINE & NORTRIPTYLINE**
      * Inhibit NET and SERT
      * Antagonist at muscarinic receptors (look like atropine)
      * Act like local anesthetic-type antiarrhythmic (class1a)
      * α1-receptor antag
      * antagonists at H1 receptors (like old fashion antihistamine)
      * Cadiotoxic and lots of antimuscarinic effects
      * Sexual side effects
      * 1 week supply could be fatal
      * mostly long DOA
      * Start w/ low dose and ↑
      * Drug interactions—**MAOI,** fluoxetine (SSRI) inhibits the biotransformation of these
  + **ATYPICAL (2ND GENERATION)**
    - *NO INTERFERENCE W/ SEXUAL FUNCTION*
    - **BUPROPION—UNCICYCLIC**
      * Inhibits DAT (and NET a little) and releases presynaptic DA and NA
      * Adverse: insomnia, agitation, and anorexia
      * Approved for smoking sessation
      * LOWERS seizure threshold
    - **MIRTAZAPINE—TETRACYCLIC**
      * α2-antagonist (blocks the normal feedback mechanism) so NE and 5-HT release are ↑
      * also antagonist at other 5-HT receptors and H1 receptors so its quite SEDATING
  + **SEROTONIN-SELECTIVE REUPTAKE INHIBITORS (SSRIS)**
    - **FLUOXETINE—MANY DRUG INTERACTIONS!!!**
      * Metabolized to norfluoxetine (active) which has longer half-life so it accumulates
      * **STRONG CYP2D6 INHIBITOR (**this metabolizes TCA’s)
    - **SERTALINE—**short acting
    - **PAROXETINE**
      * **STRONG CYP2D6 INHIBITOR**
      * short acting
    - **CITALOPRAM**
    - All of these selective for SERT
    - No myocardial effects, much safer in OD
    - 1st drug tried in new patients
    - Adverse effects associated w/ ↑ 5-HT
      * N/D, GI upset, Impaired sexual function and interest (more than w/ TCA), HA, insomnia
      * Serotonin Syndrome—DANGEROUS (get it when you use w/ MAOI or OD on drug)
        + Altered mental status, sweating, fever, tremor, myoclonus
      * Discontinuation Syndrome—more obvious w/ shorter t1/2 like (sertraline and paroxetine)-🡪 dizziness and paresthesias
    - ↓ risk of suicide
  + **SEROTONIN-NONSELECTIVE REUPTAKE INHIBITOR (SNRI)**
    - **DULOXETINE**
    - **VENLAFAXINE**
      * Biotransformed to desvenlafaxine which is active
      * CARDIOTOXIC
    - Both inhibit SERT and NET
    - No direct cardiac tox
    - Safer than TCA in OD but venlafaxine has MORE CARDIOTOX than SSRI!
    - Adverse: ↑ HR and BP, insomnia, anxiety, discontinuation syndrome
    - ↓ risk of suicide
  + **5-HT ANATAGONIST**
    - **TRAZODONE—**not commonly used
    - **NEFAZODONE—**never used
    - Significant sedation—sometimes used an a hypnotic
  + **MAO INHIBITOR—***long acting, irreversible inhibitors!*
    - **SELEGILINE**
      * Used also in tx of Parkinson dz
      * Selective for MOA-B
      * Drug and food interactions is less of a problem
    - **TRANYLCYPROMINE**
    - Both are irreversible inhibitors. Slow TOA (requires resynthesis of enzyme)
    - Used in patients unresp. To other drugs
    - LOTS OF DRUG INTERACTIONS and FOOD INTERACTIONS
      * Drugs
        + OTC: Cold and cough meds, Nasal decongestants, Hay-fever meds, Sinus meds, Asthma inhalants, Anti-appetitite meds, Wt ↓ preps, L-tryptophan containing preps
        + Rx: Meperidine, buspirone (HTN) amitriptyline, nortriptyline, carbamazepine, cyclobenzaprine, TCA’s, SSRI’s, SNRI’s, tyramine (HTN crisis), levodopa (HTN crisis)
      * Food—liver, fava beans, sauerkraut, cheese, yogurt, beer and wine, chocolate, caffeine
    - Adverse: HA, drowsiness, wt gain, postural hypotension, sexual dysfunction, agitation and insomnia
    - OD: agitation, delirium, seizures, coma, shock, hyperthermia
    - Withdrawal rxn: axiety, sweating, HA
  + **MOOD STABILIZORS**
    - **LITHIUM**
      * Used for bipolar (manic), acute mania, and to prevent relapse of bipolar
      * Narrow therapeutic window
      * In the body it is handled like Na (excretion even depend on Na intake)--↓ Na intake🡪 serious toxicity
        + Any ↓ in Na will lead to Li+ accumulation (diuresis, diarrhea, dehydration)
      * Clearance is ↓ during pregnancy
      * 2-3 weeks until see effects
      * Mech: affects NE and 5-HT neurotransmission--↓ availability of IP3
      * Adverse: Tremor, polyuria and thirst (↓ kidney’s response to vasopressin🡪 nephrogenic diabetes insipidus. Responds to amiloride), edema, wt gain, fatigue, weakness, HA, confusion, memory impairment, ↓ thyroid function, ↓ SA node function, acne like skin eruptions, Leukocytosis (looks like infection but it isn’t), N/V anorexia
      * As levels ↑ 🡪 ECG changes (arrhythmias🡪 sudden death), hypotension, incoordination, course tremor, ataxia, tinnitus, minor seizure activity, generalized seizures, coma, DEATH
    - **VALPROIC ACID**
      * Liver toxic
    - **CARBAMAZEPINE**
      * Induces its own metabolism and the metabolism
* **ANTI-EPILEPTICS** (limit seizure spread)
  + *Epilepsy ↑ risk to fetus so tx pregnant women w/ epilepsy*
  + **NA+ CHANNEL BLOCKER ANTIEPILEPTICS**
    - **PHENYTOIN**
      * Partial, generalized tonic-clonic seizures (NOT absence)
      * Prolongs the time the voltage gated Na channel is in the inactivate state which makes the neurons refractory period longer🡪 limits ability to transmit series of AP’s
      * Slow abs from GIT—once absorbed HIGHLY PROTEIN BOUND (drug interactions)
      * Elim—met to inactive then its glucuronidated
        + ENZYMES IS EASILY SATURATED—goes from 1st order to 0 order (high conc.) –dose concentration curve is not linear.
      * Adverse: nystagmus, ataxia, vertigo, diplopia, sedation, others—Gingival hyperplasia, hirsutism, lymphadenopathy, ↓ vit D metabolism—bone malformation, periph neuropathy
      * Fetal hydantoin syndrome (all AED’s)
      * Interactions: drugs that are highly protein bound, competition for hepatic enzymes, induction of hepatic enzymes
    - **FOSPHENYTOIN**
      * --water soluble pro-drug for IV or IM use
      * Adverse--HYPOTENSION
    - **CARBAMAZEPINE**
      * Prolongs Na channel inactivation
      * Use: partial, generalized tonic-clonic (not absence), anti-manic, trigeminal neuralgia
      * INDUCES ITS OWN METABOLISM--↓ its own half life.
        + Also induce metabolism of other AED’s, oral contraceptive
        + Biotransformation of this drug is inhibited by grapefruit juice🡪 ↑ bioavailability
      * Adverse: dose related—ataxia, vertigo, diplopia, idiosyncratic reactions like aplastic anemia, agranulocytosis, skin rash
    - **VALPROIC ACID**
      * Inhibits Ca currents in thalamic, prolong Na channel inactivation, and affects synthesis and breakdown of GABA (not in humans)
      * Use: Absense, myoclonic epilespsy, generalized tonic-clonic (grand mal)
      * Also used to treat bipolar disorder (TWO WORDS so BI-polar) and as prophylaxis for migraines
      * 90% protein bound (drug interactions w/ warfarin)
        + displaces phenytoin from plasma proteins!!!
        + Inhibits metabolism of several drugs (phenytoin, carbamazepine, phenobarbital, lamotrigine)

B/c it inhibits CYP2C9

* + - * + Adverse: **NO SEDATION,** GI irritation, weight gain, tremor, hair loss, LIVER TOX/HEPATITIS in kids <2 and when used w/ other AEDs, TERATOGENIC
    - **LAMOTRIGINE (LA MOAT GAVE ME A RASH!!---STEVE IS A LAM-O)**
      * Adjunct in partial or generalized seizures, also used in absence epilepsy
      * Prolongs Na channel inactivation
        + and has some actions to some types of voltage-gated Ca channels
      * Adverse—LIFE THREATENING RASH!! –can progress to stevens johnsons syndrome
  + **ENHANCE GABA**
    - **BENZODIAZEPINES**
      * **CLONAZEPAM**
        + 2nd line drug for partial, absence, myoclonic seizures and infantile myoclonic spasms
        + Adverse: SEDATION and tolerance
      * **DIAZEPAM/LORAZEPAM**
        + STATUS EPILEPTICUS—emergency situation

Tx suspicion: Airway, breathing, circulation, Give drug IV, Benzo then follow w/ IV fosphenytoin

* + - * + Risk—too much effect—respiratory depression!
    - **BARBITURATES**
      * **PHENOBARBITAL**
        + Use: partial seizures, many generalized seizures (not absence)
        + ↑ GABA actions at GABAA
        + more selective AED than other barbituates
        + SEDATION is a problem
        + May see hyperactivity in kids
  + **T-TYPE CA2+ CHANNEL**
    - **ETHOSUXIMIDE—**TREVOR SUX AT MAKING UP MNEUMONICS
    - FOR ABSENSE SEIZURES
    - Inhibits T-type voltage gated Ca channels in thalamus
    - Adverse: GI distress, sedation (usually limited factor)
  + **INHIBIT EXCITATORY NT RELEASE**
    - **GABAPENTIN (Α2Δ)**
      * Use: partial seizures, generalized tonic-clinic seizures also post-herpetic neuralgia
      * Other uses: diabetic and other painful neuropathy
      * Mech: inhibit function of presynaptic voltage gated Ca channels--↓ release of glutamate
  + OTHER TX MODALITIES
    - Vagal N. stimulation
    - Ketogenic diet (high in fat, low in carbs and protein🡪 ketosis)
    - Surgical

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* **SPASMOLYTIC DRUGS**
  + **BACLOFEN**—↑ inhibition
    - Antagonist at GABAB receptors🡪 ↑ K+ conductance🡪 hyperpol of the neuron
    - Adverse—sedation, withdrawal seizure
  + **DANTROLENE**—inhibit Ca release from ryanodine receptors on the SR
    - Used to tx malignany hyperthermia (using succinylcholine and halothane together)
    - Adverse: sedation and muscle weakness
  + **DIAZEPAM** 
    - Enhance GABAA effects at their receptors. Actions in SC as well as BS
  + **CYCLOBENZAPRINE**—alter descending tone
    - Significant anti-muscarinic effects
    - Adverse: sedation, confusion
  + **BOTULINUM TOXIN**—block Ach release from nerve terminals
    - Used for wrinkles and spastic disorders like cerebral palsy
* **DRUGS OF ABUSE**
  + **OPIOIDS**
  + **SEDATIVE-HYPNOTICS**
  + **ETHANOL**
  + **BENZODIAZEPINES**
  + **VOLATILE INTOXICANTS**
  + **AMPHETAMINE TYPE STIMULANTS**
  + **COCAINE**
  + **CAFFEINE**
  + **HALLUCINOGENS, PHENCYCLIDINE, MARIJUANA**
  + **NICOTINE**